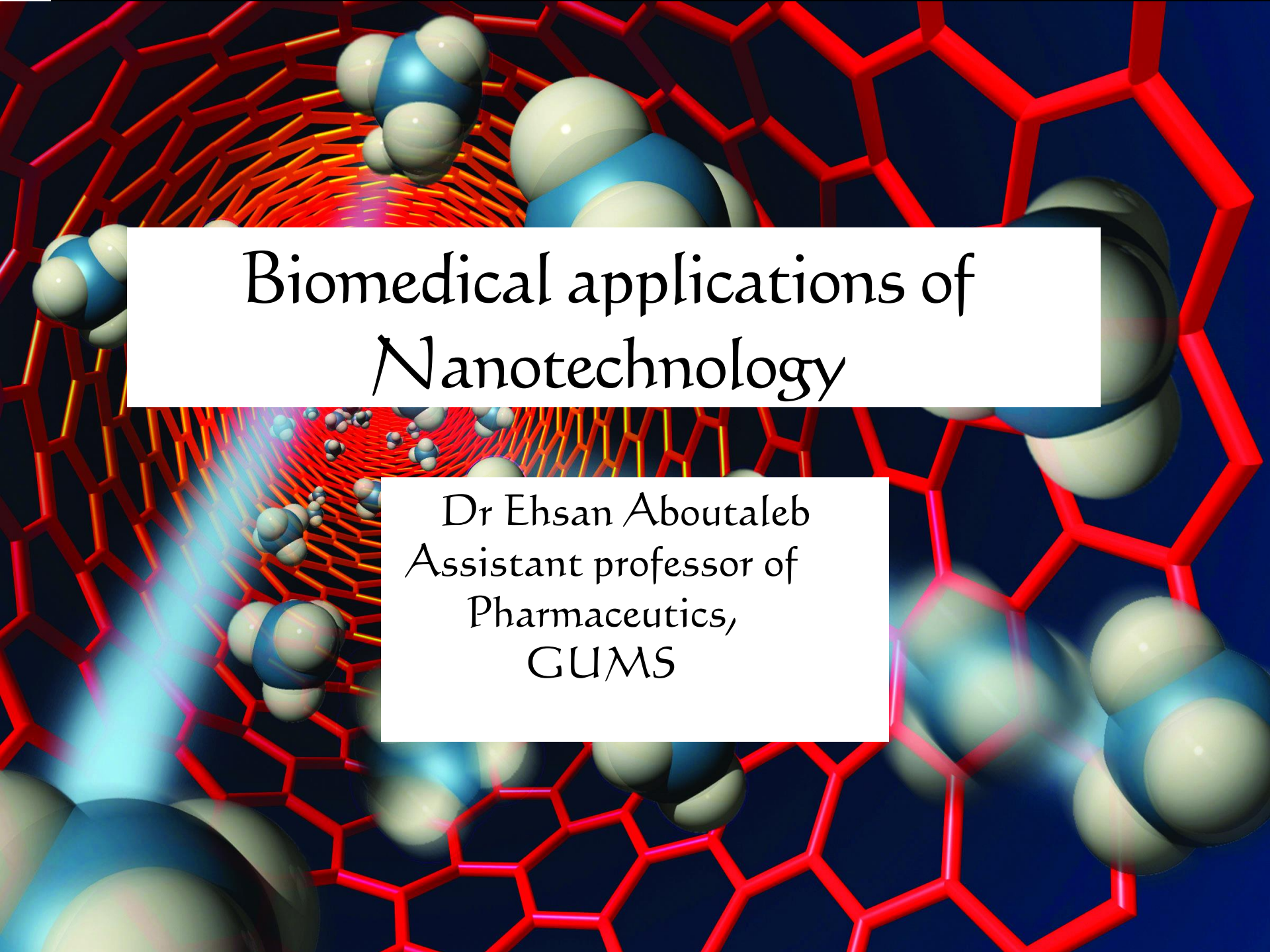
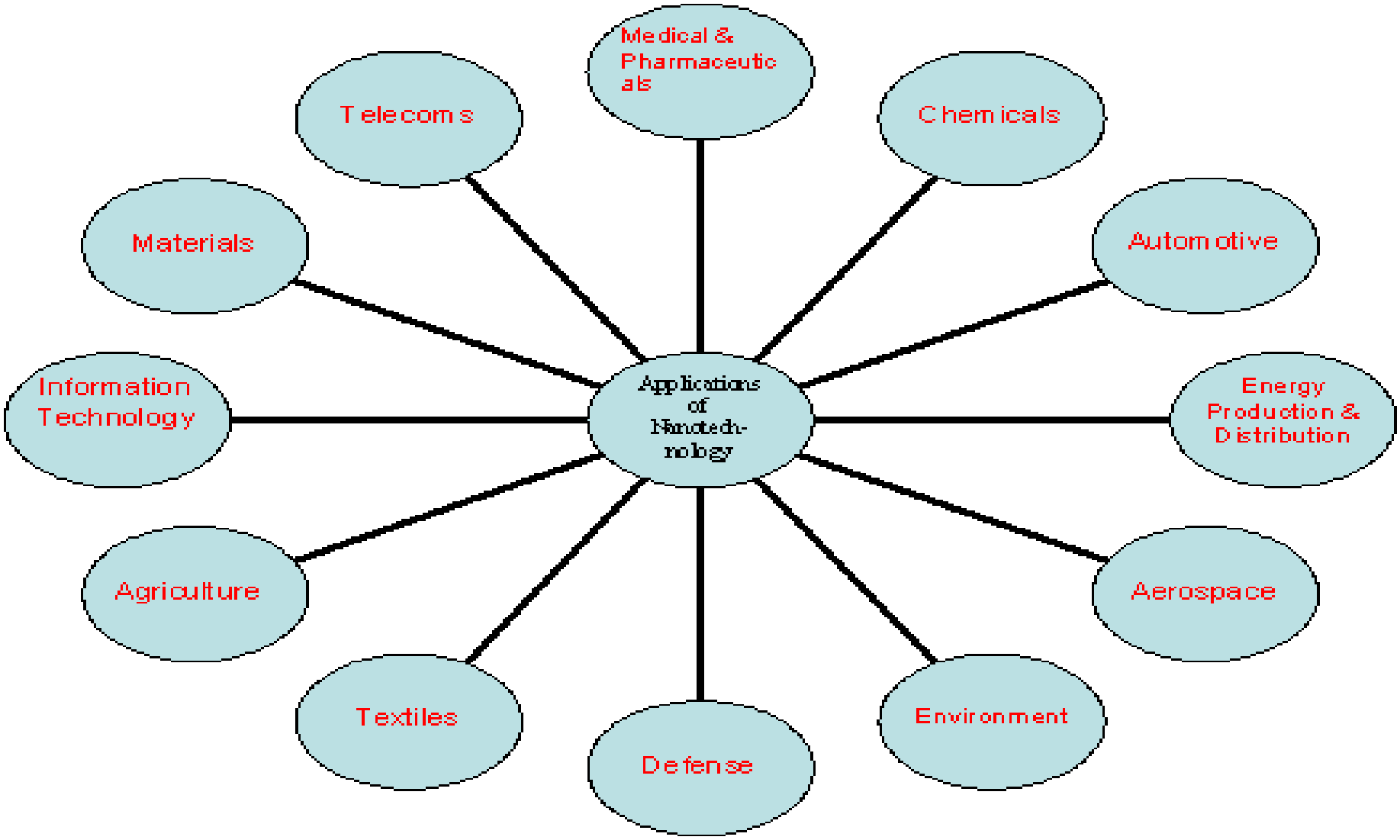


Biomedical applications of Nanotechnology

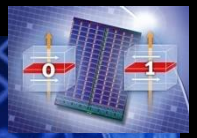
Dr Ehsan Aboutaleb
Assistant professor of Pharmaceutics,
GUMS

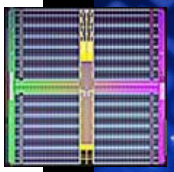
Applications of Nanotechnology

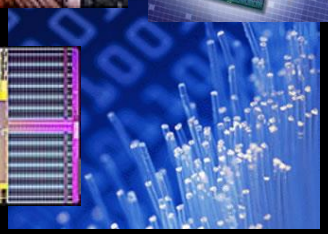


Nanotechnology Applications

Information Technology







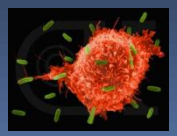
- Smaller, faster, more energy efficient and powerful computing and other IT-based systems

Energy

- More efficient and cost effective technologies for energy production
  - Solar cells
  - Fuel cells
  - Batteries
  - Bio fuels

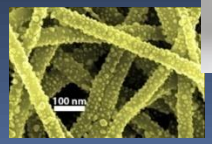
Medicine

- Cancer treatment
- Bone treatment
- Drug delivery
- Appetite control
- Drug development
- Medical tools
- Diagnostic tests
- Imaging



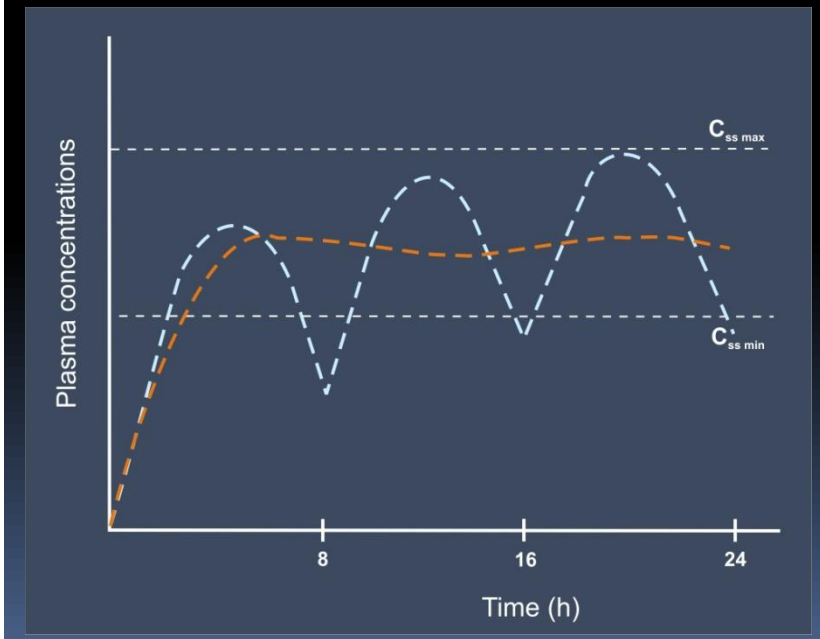
Consumer Goods

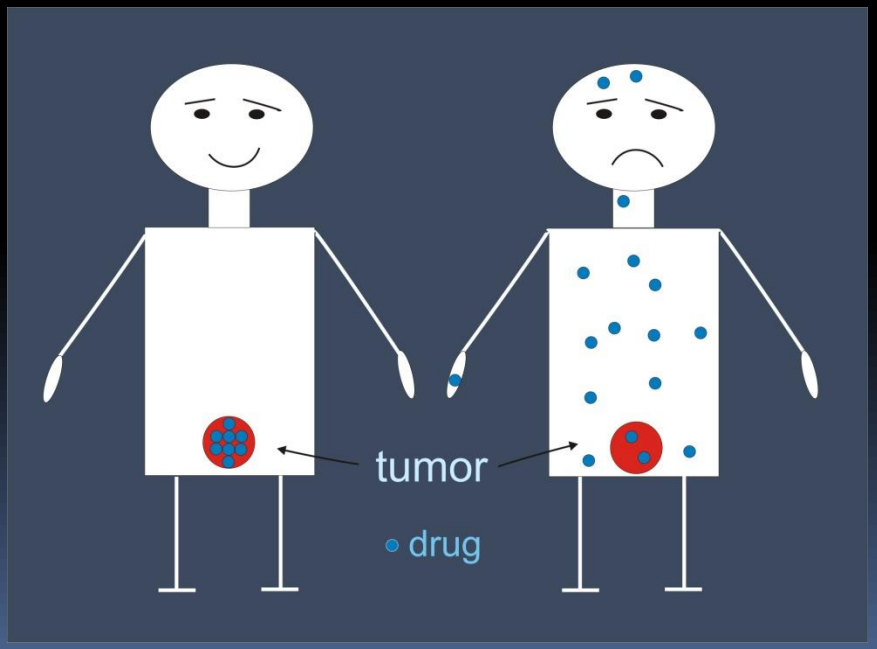
- Foods and beverages
  - Advanced packaging materials, sensors, and lab-on-chips for food quality testing
- Appliances and textiles
  - Stain proof, water proof and wrinkle free textiles
- Household and cosmetics
  - Self-cleaning and scratch free products, paints, and better cosmetics



Generations of dosage forms

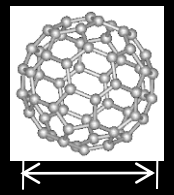
- 1st gen. – conventional (unmodified) release of API
- 2nd gen. – controlled release of API (CR)
- 3rd gen. – targeted distribution drug delivery systems





What is Nanoscale

Fullerenes C_{60}



www.physics.ucr.edu

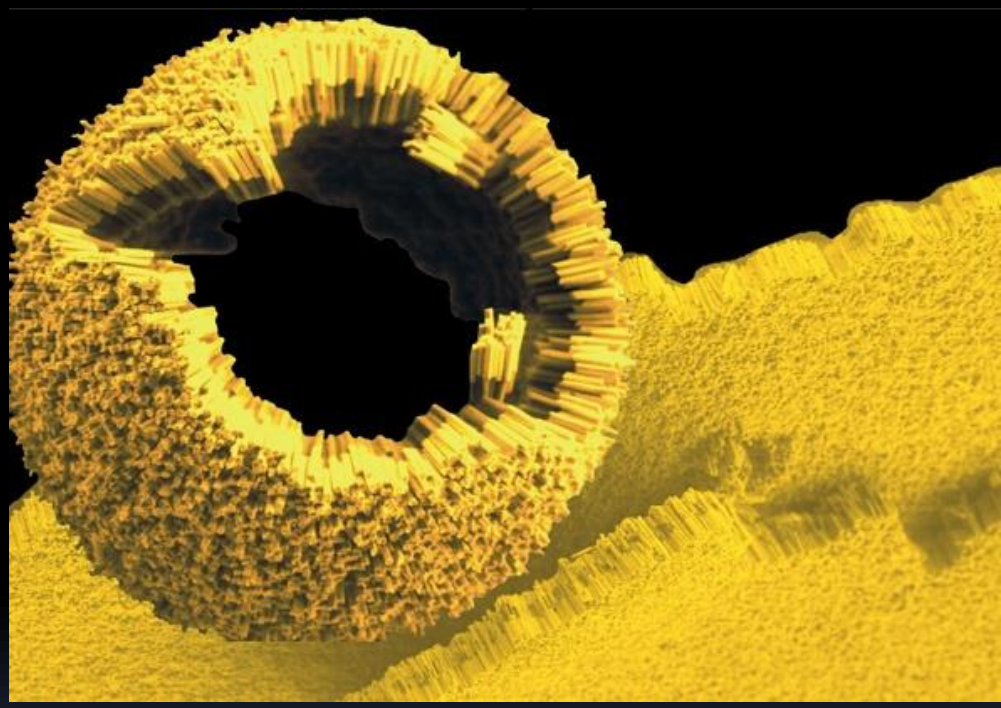
1.27 × 107 m → **0.22 m** → **0.7 × 10-9 m**

10 millions times smaller

1 billion times smaller

Nanoparticles for Drug Delivery

- Gold Nanoshells
- Quantum Dots
- PLGA Particles
- Dendrimers
- Carbon Nanotubules
- Liposomes
- Niosomes
- Solid lipid nanoparticles
- Superparamagnetic

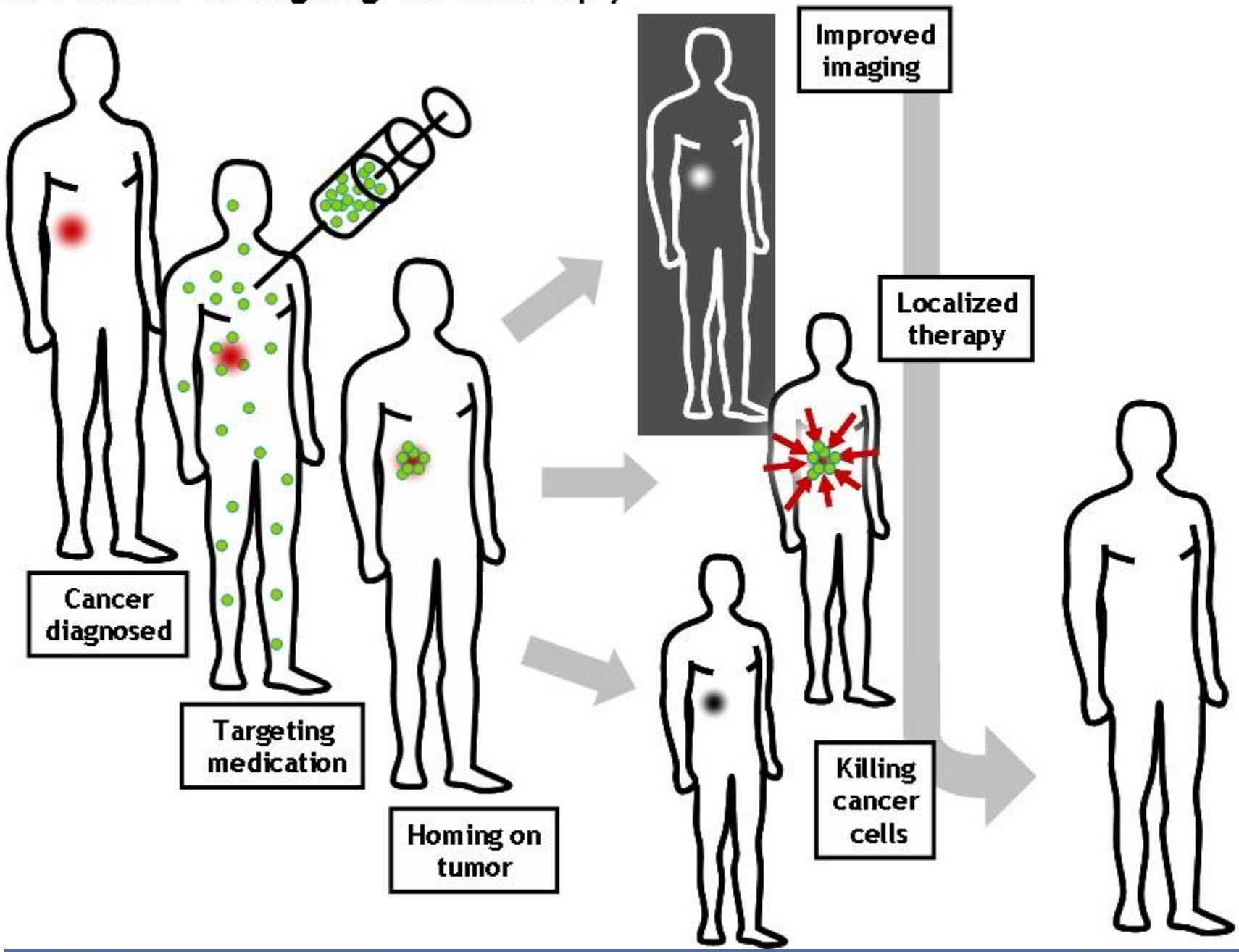


Nanoparticles

- Small solid particle that range from 10-500 nm
  - Nanoparticles are generally used as carriers for therapeutic or diagnostic agents
  - Can be solid or hollow
  - Composed of lipids, poly-lactic acid

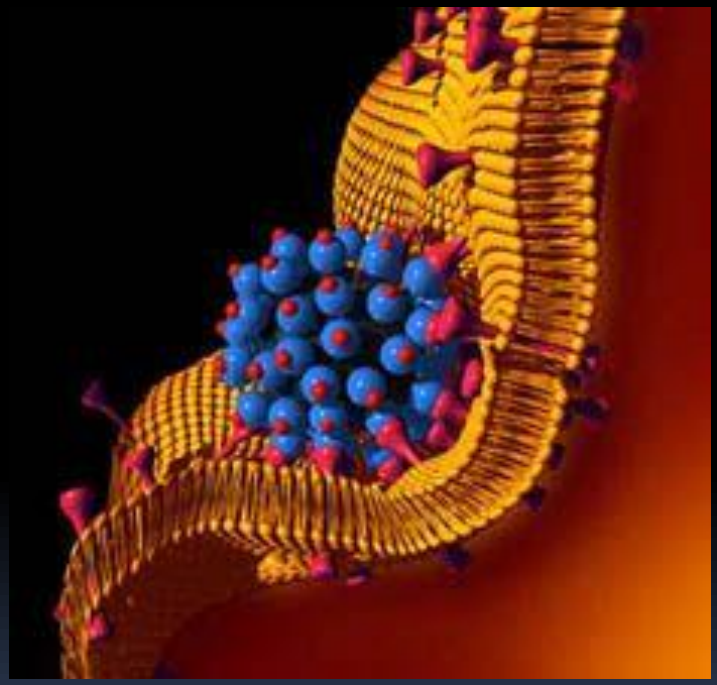
    gold shells, dendrimers, Cad/Selenium
- Highly stable

Molecular imaging & therapy

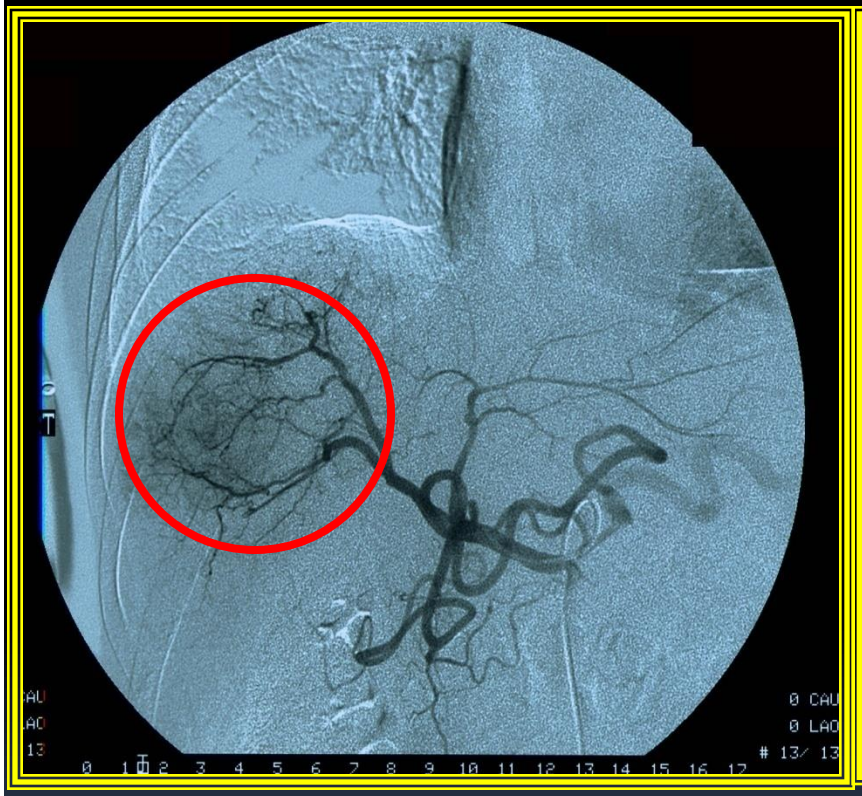


Targeted Drug Delivery

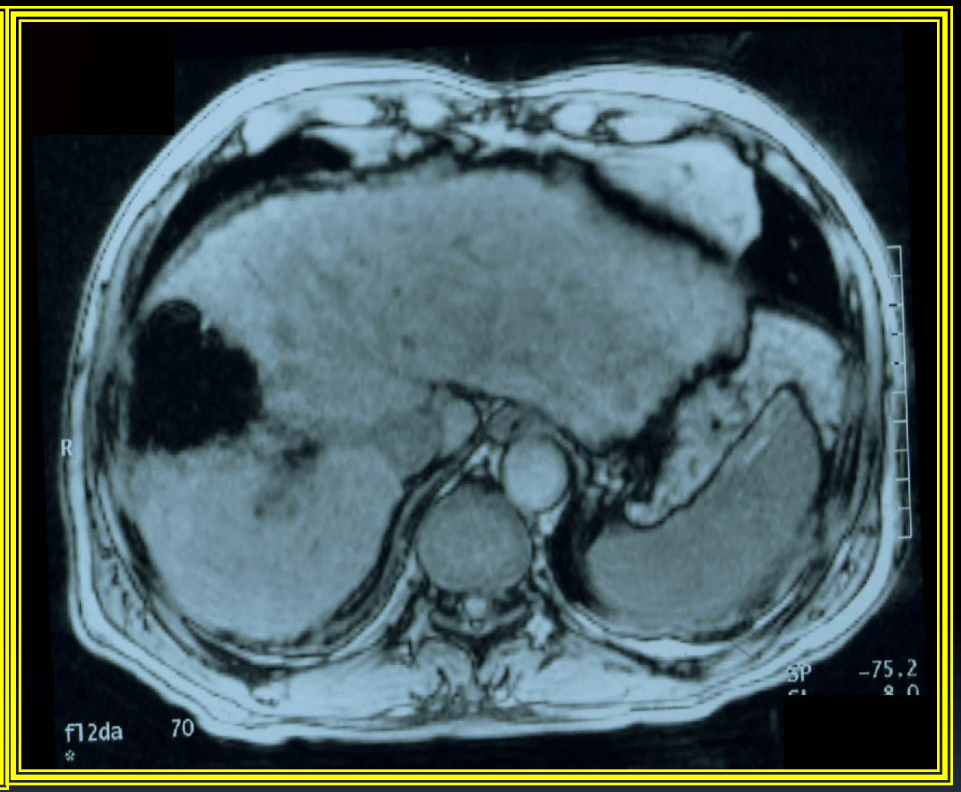
- Active targeting
- Passive targeting



Passive Targeting

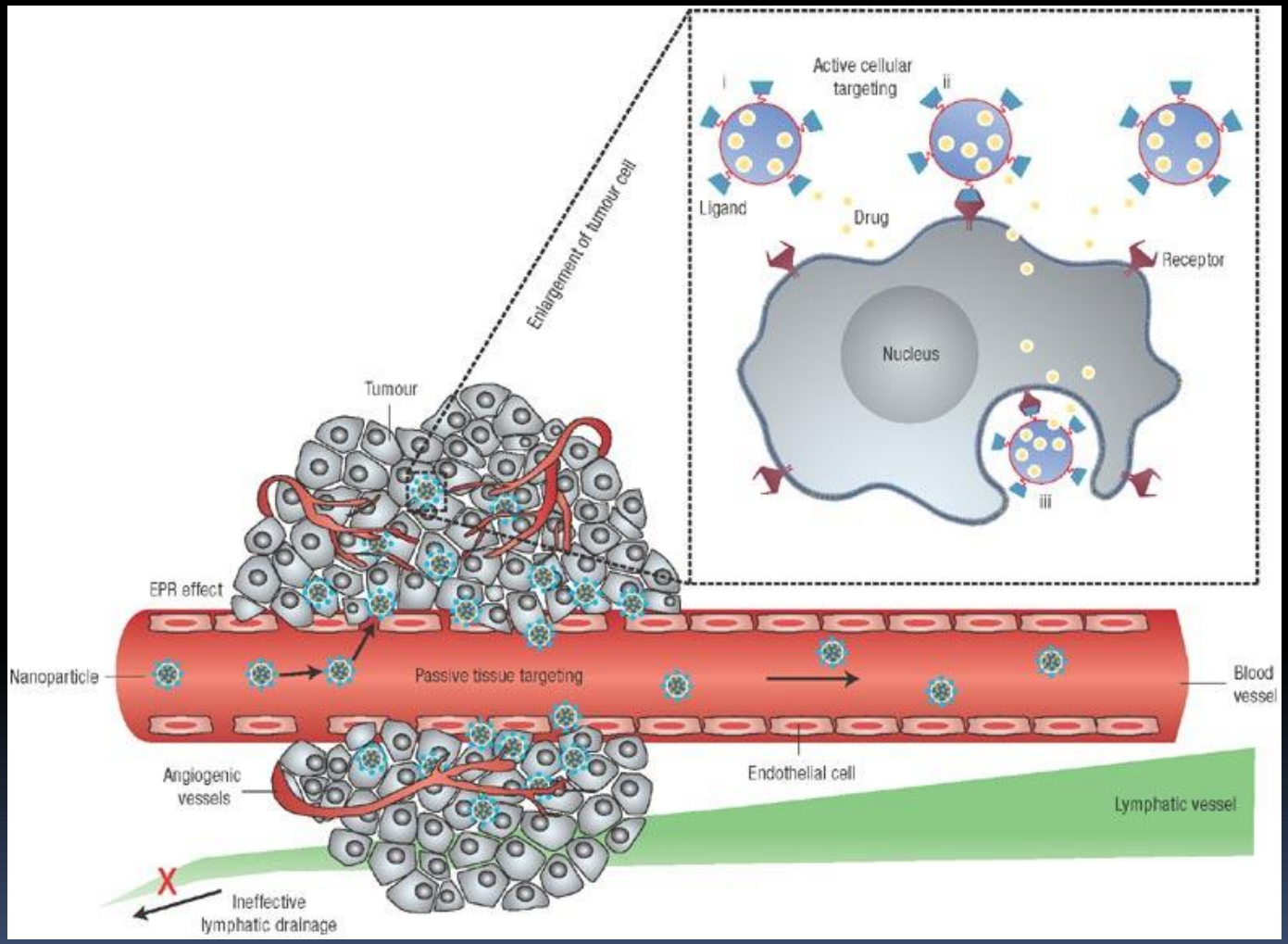


Angiogram of Vessels



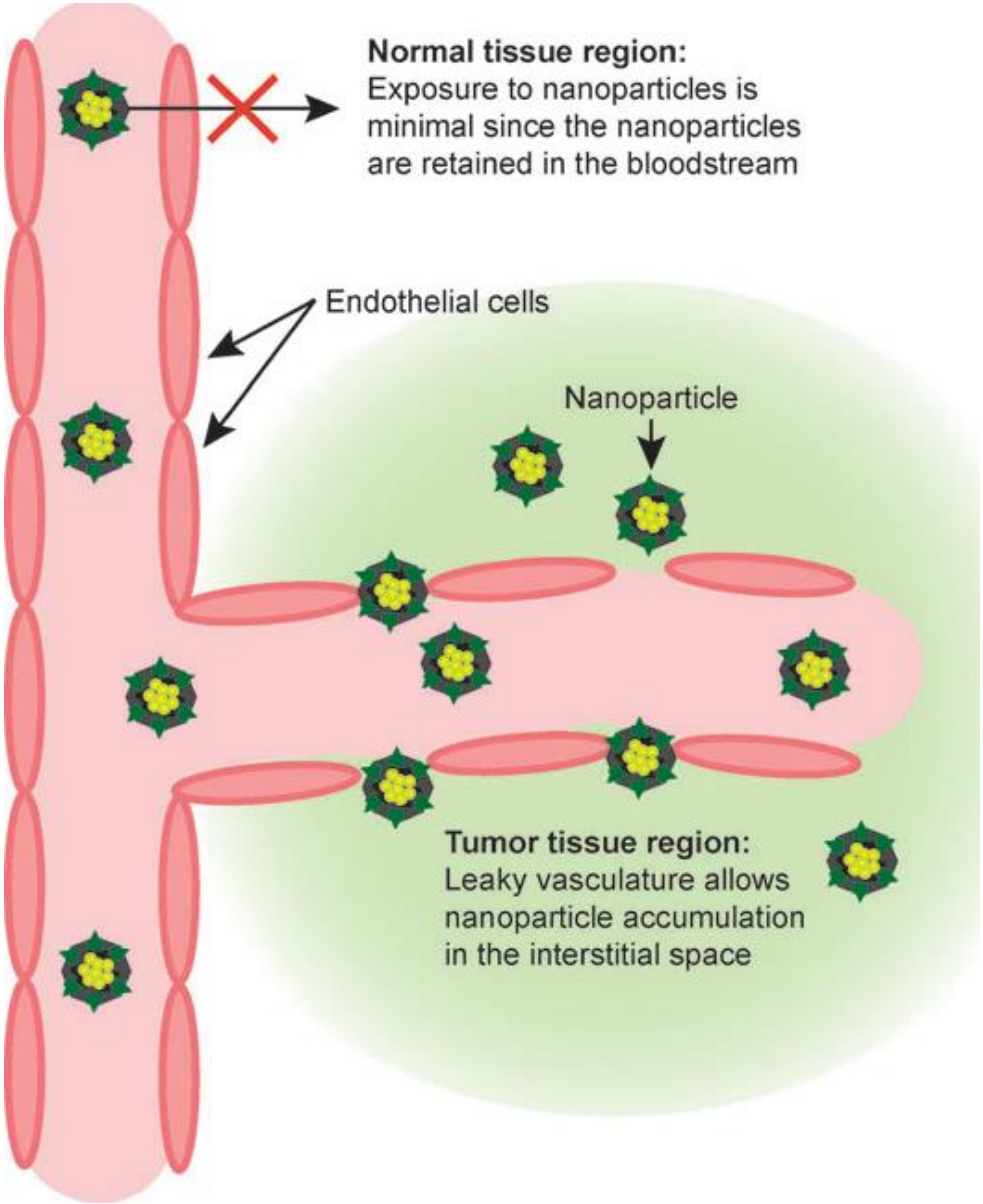
MRI

The EPR effect



- Enhanced permeability and retention

EPR: Taking advantage of retention



A. Tumorous tissues suffer of Enhanced Permeability and Retention effect (RES)

B. Nanoparticles injected in the blood stream do not permeate through healthy tissues

C. Blood vessels in the surrounding of tumorous tissues are defective and porous

D. Nanoparticles injected in the blood permeate through blood vessels toward tumorous tissues, wherein they accumulate

Annu. Rev. Biomed. Eng. 2007. Vol. 9, pp. 257–88

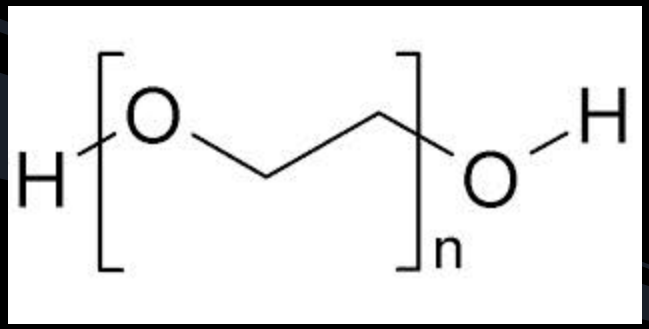
The RES System

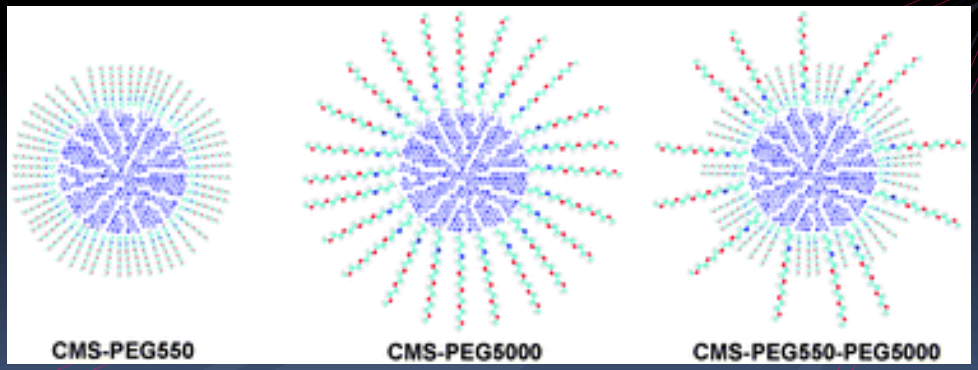
RES Captures

- NPs of more than 300nm
- Hydrophobic Surface
- 75% of dose goes to Liver

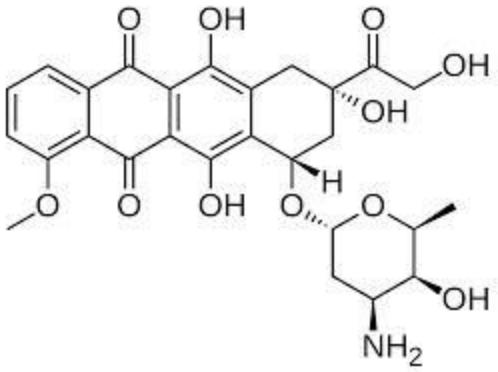
PEGylation

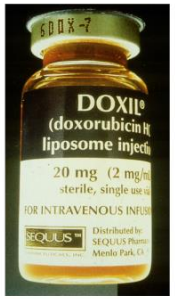
Stealth nanoparticles



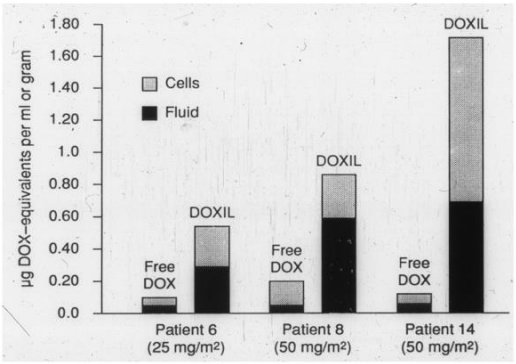


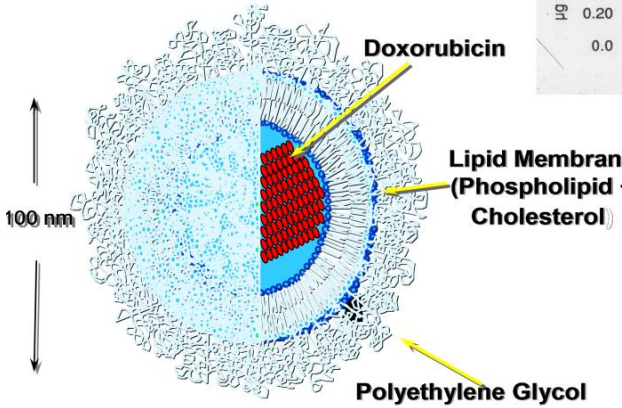
Clinical Example of EPR

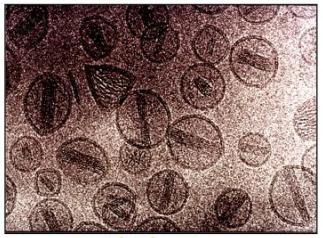




DOXIL





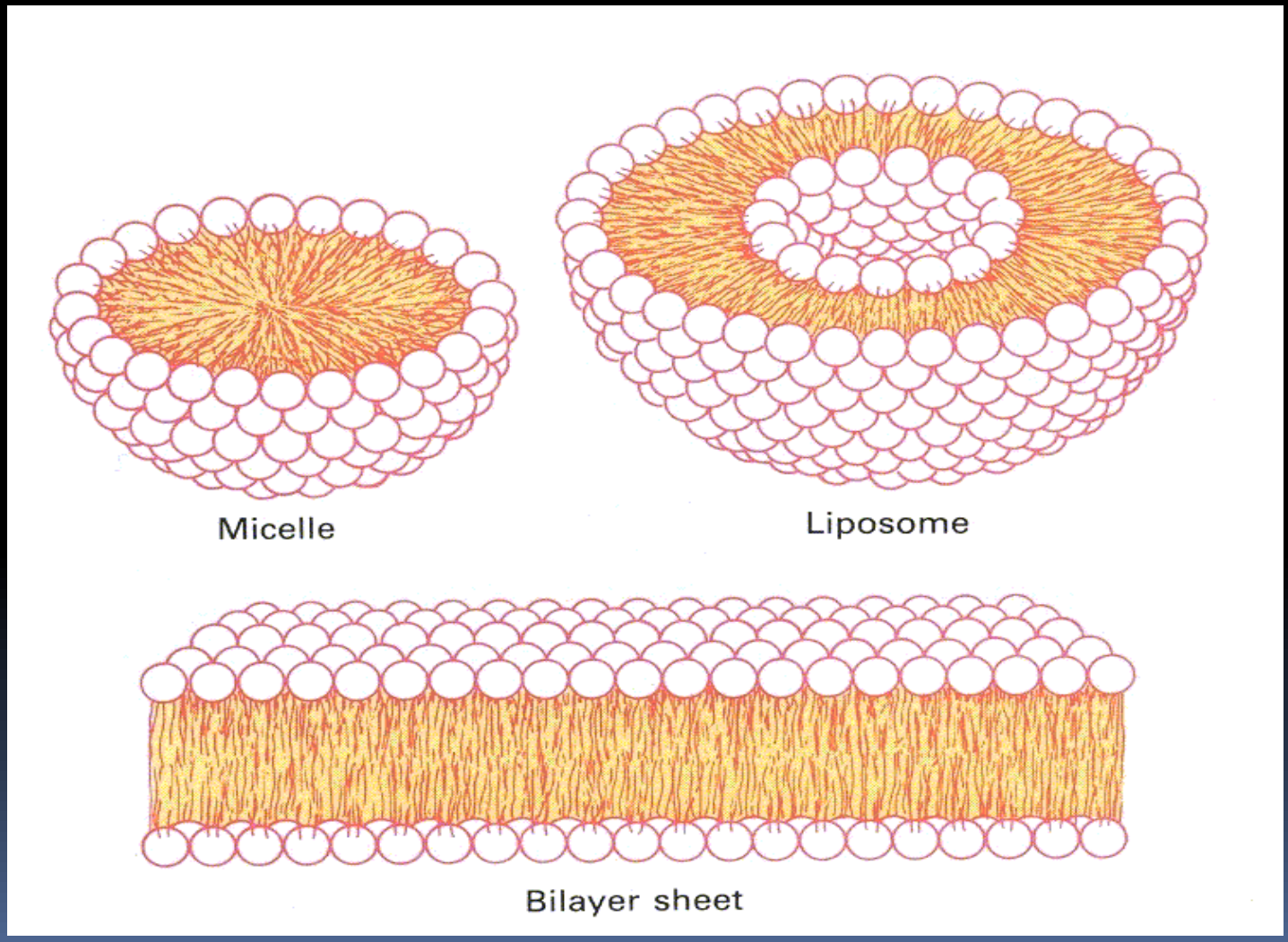

morphology

Doxil is a polyethylene glycol coated liposomal formulation of doxorubicin.

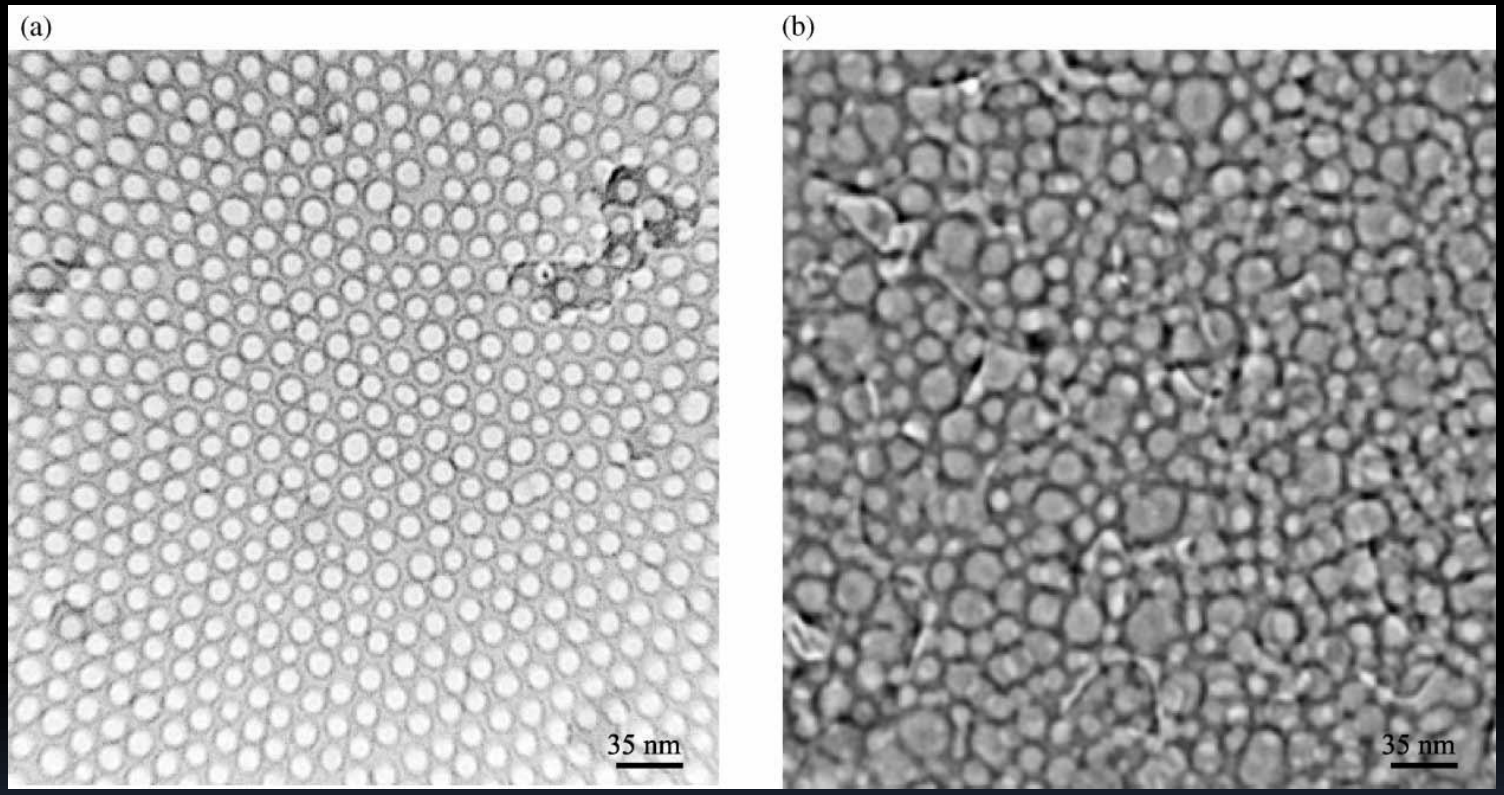
Marketed by Ben Venue Laboratories of J&J. Outside the US, Doxil is known as Caelyx (Janssen).

Approved by the FDA for treatment of ovarian cancer and multiple myeloma and an AIDS-related cancer.

Liposome and micelle

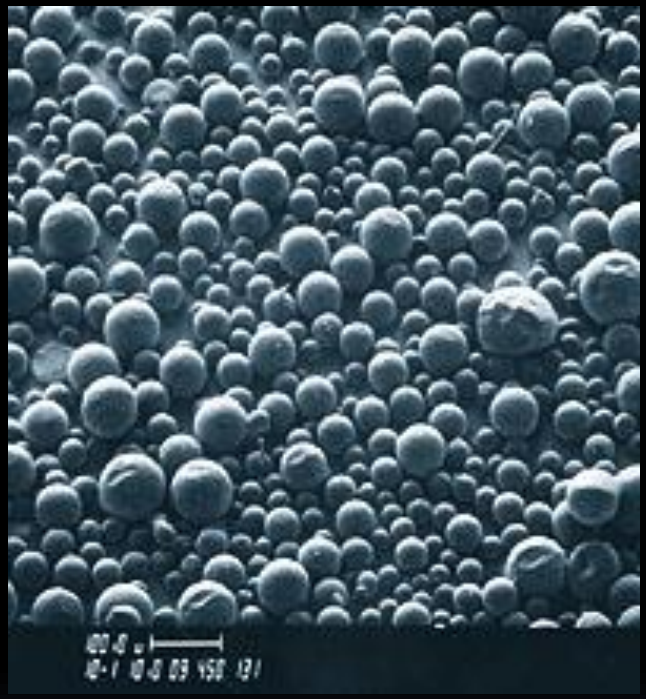


Liposome



PLGA NPs

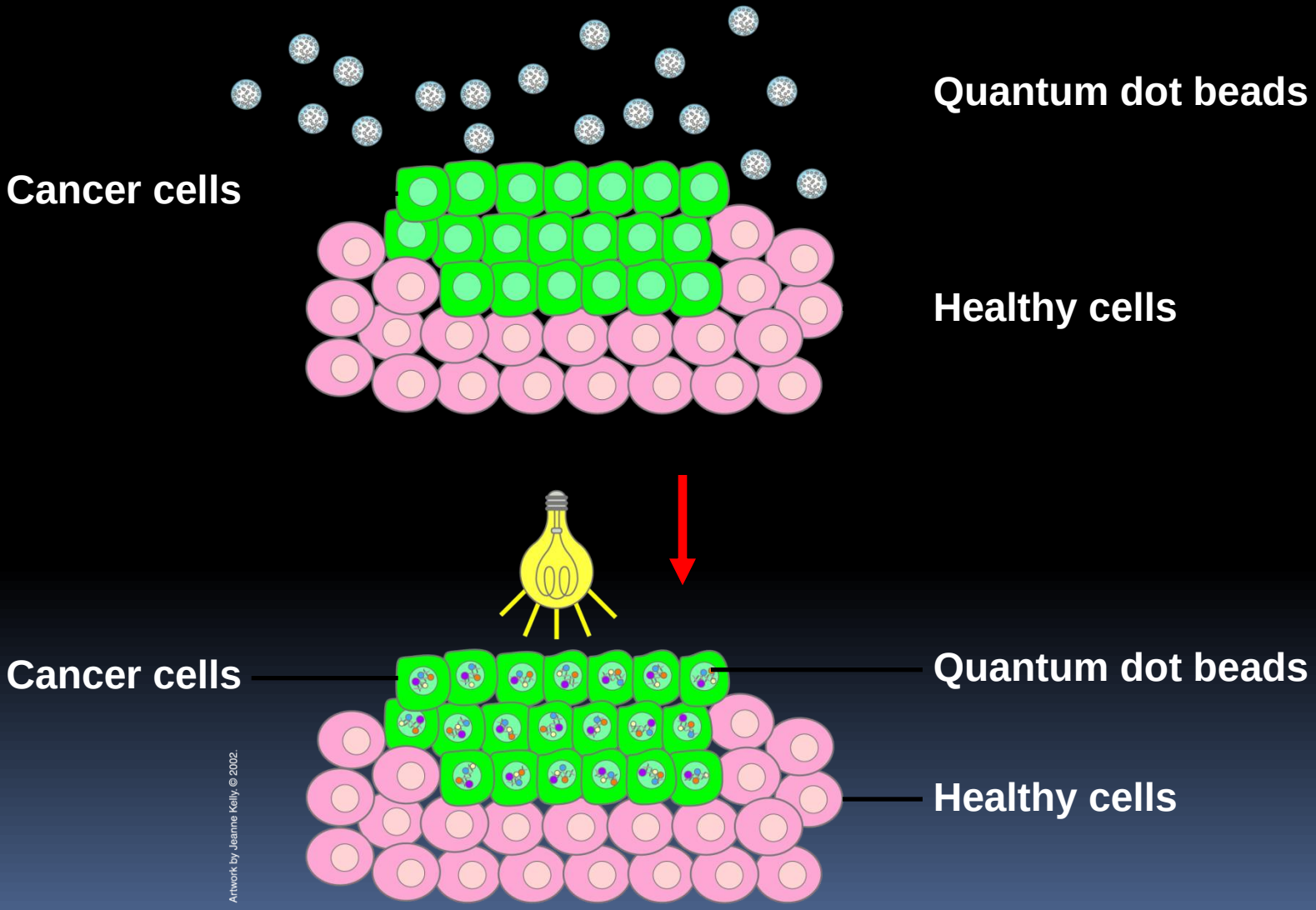
- Low toxicity
- Low cost
- High loading capacity
- Easy to make



Quantum Dots

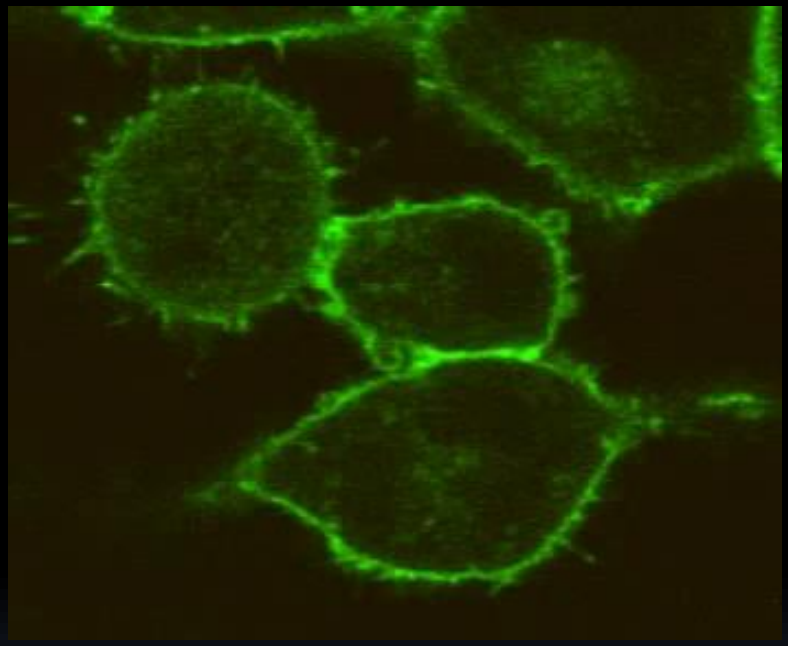
- QDs = Semiconductor nanoparticles
  - selenide core
  - zinc-sulfide shell
- Extremely small in size
  - emit light when in contact with infrared light
- QDs may emit light in one of ten different colors
  - Color changes with size

Quantum Dots Can Find Cancer Signatures



Quantum Dots in action

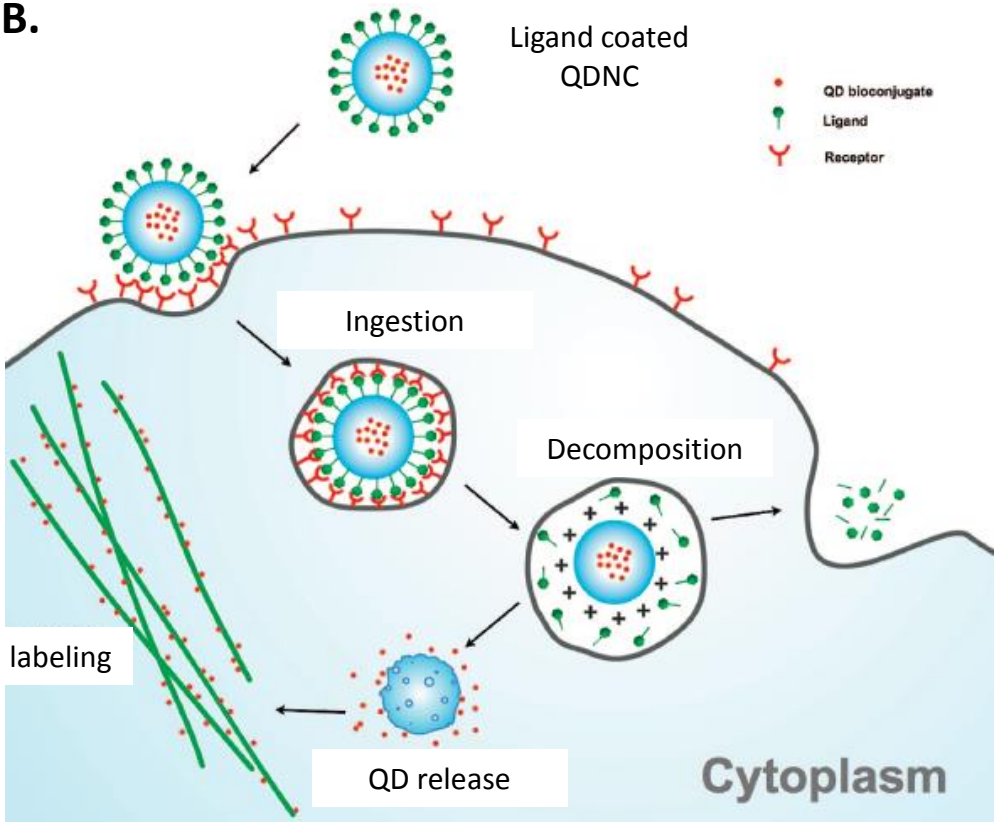
- Continuous confocal laser scanning microscopy
- QD ligands seek target cells
- Infrared light causes QDs to emit fluorescent colors

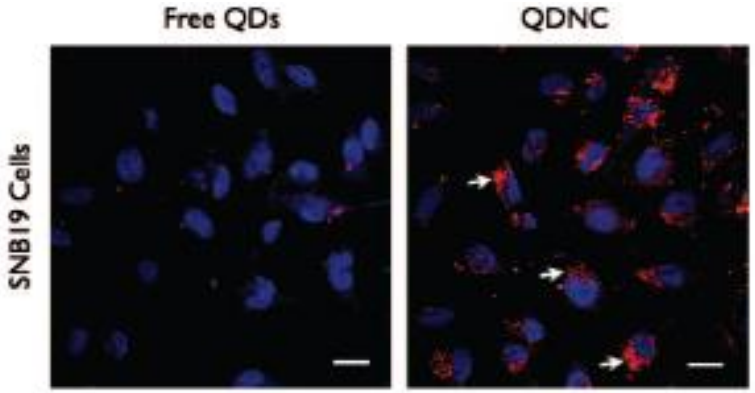


Targeting QD's for intracellular imaging

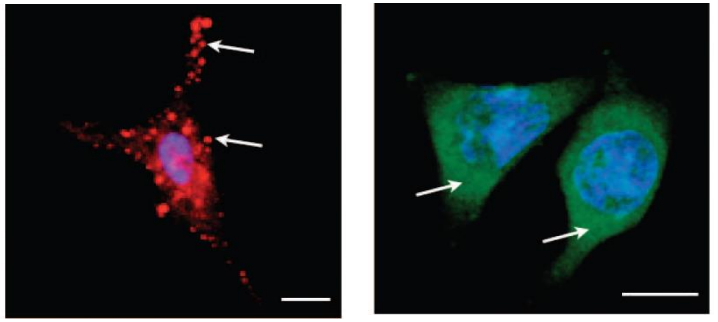
A. Using a drug-delivery-like mechanism, a targeted lipid-based nanoparticle (TNP) encapsulating QD's specifically 'attacks' a cell having the receptors that pair with its ligand coating. Upon ingestion and destruction of the TNP, the QD's are set free and accumulate on intracellular structures

B.





C. *QD (red)intracellular uptake is enhanced when using the QDNC instead of the free QD's*



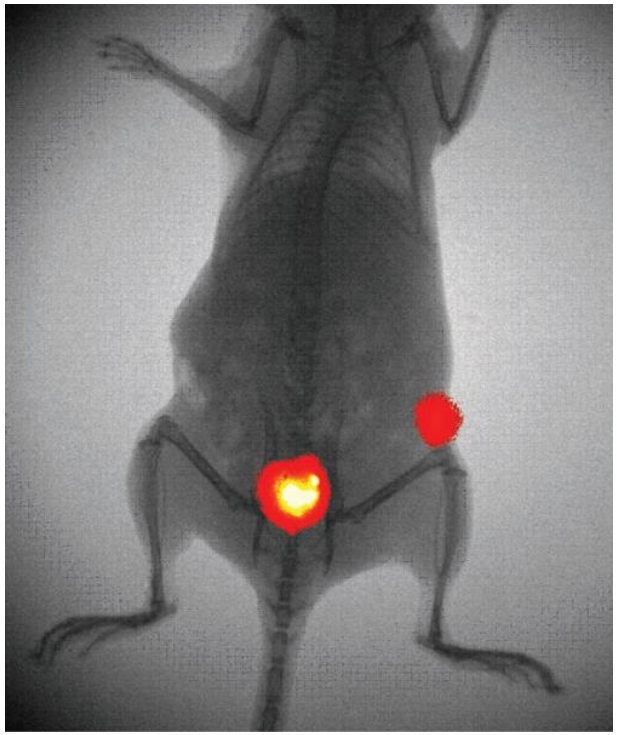
D. *Imaging of nucleus (blue) and cytoplasm (other) after 30 min (left) and 3 hours after uptake*

Nano Letters 2008., Vol. 8, pp3887-3892

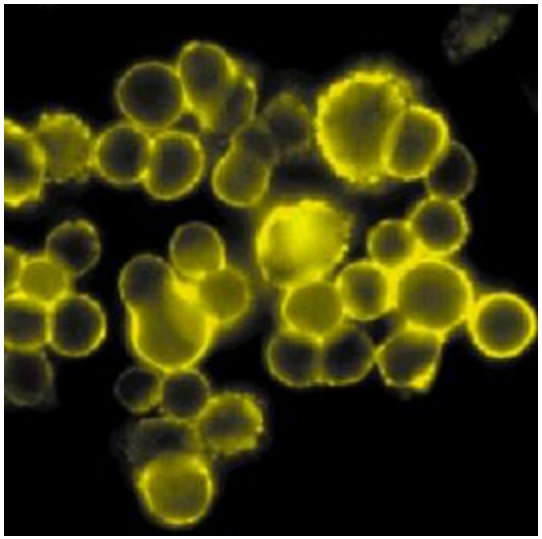
QD Localization of a Tumor

A. It is possible to overlap X-ray images with infrared images to localize a tumor. The X-ray images give the images an anatomical context, while the infrared images detect the QD's emission, which correlates to the tumor location (see B.)

B.



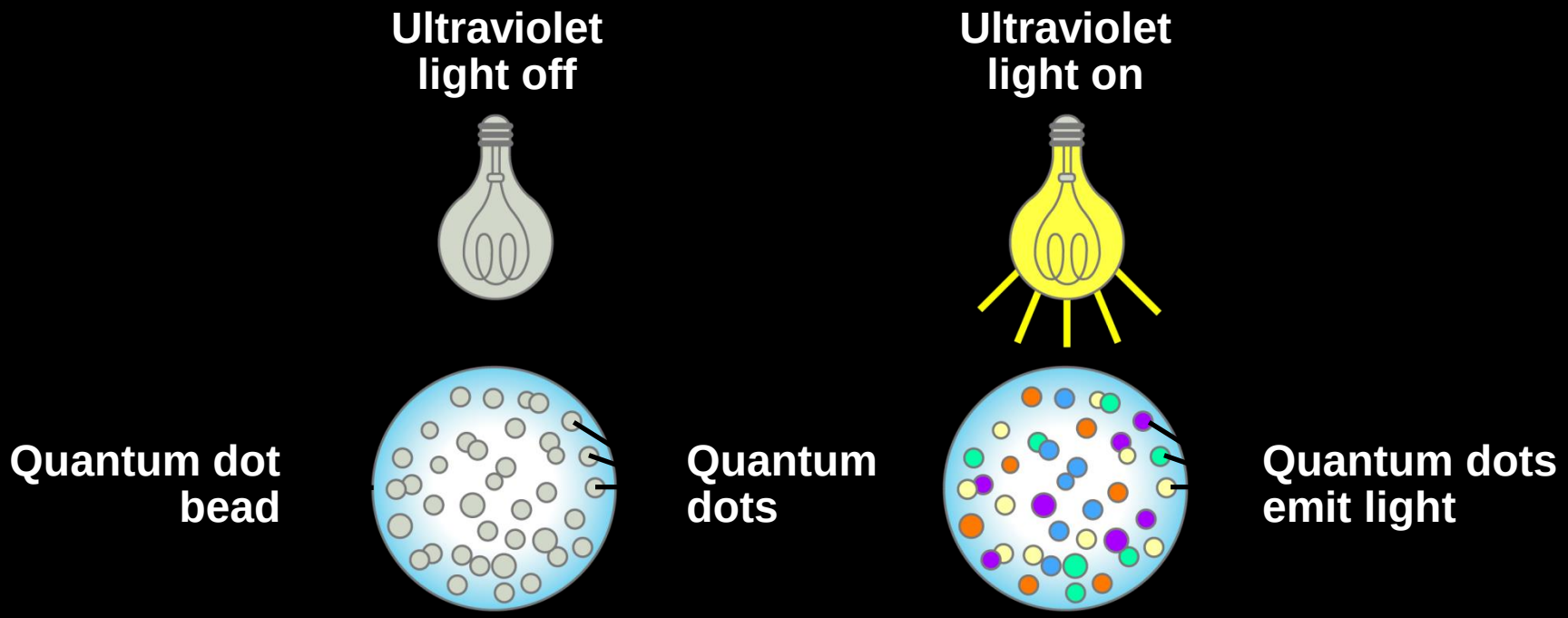
C. 560-QD-Streptadivin targets and images In-vitro breast cancer cells having the IgG factor characteristic of chemotherapy responsive cells

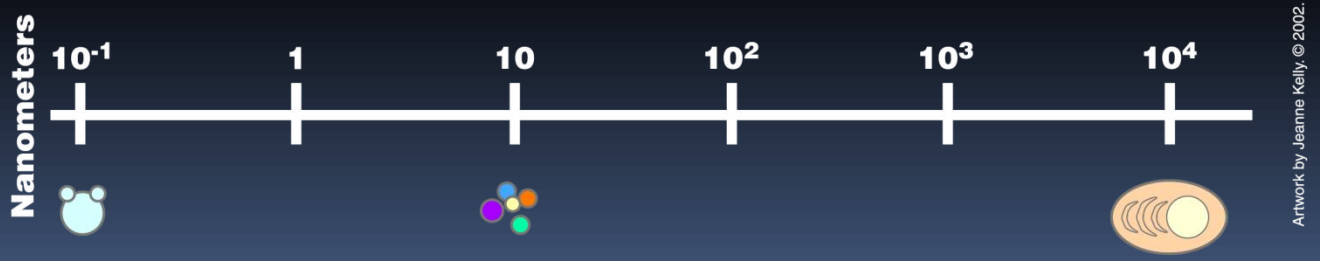


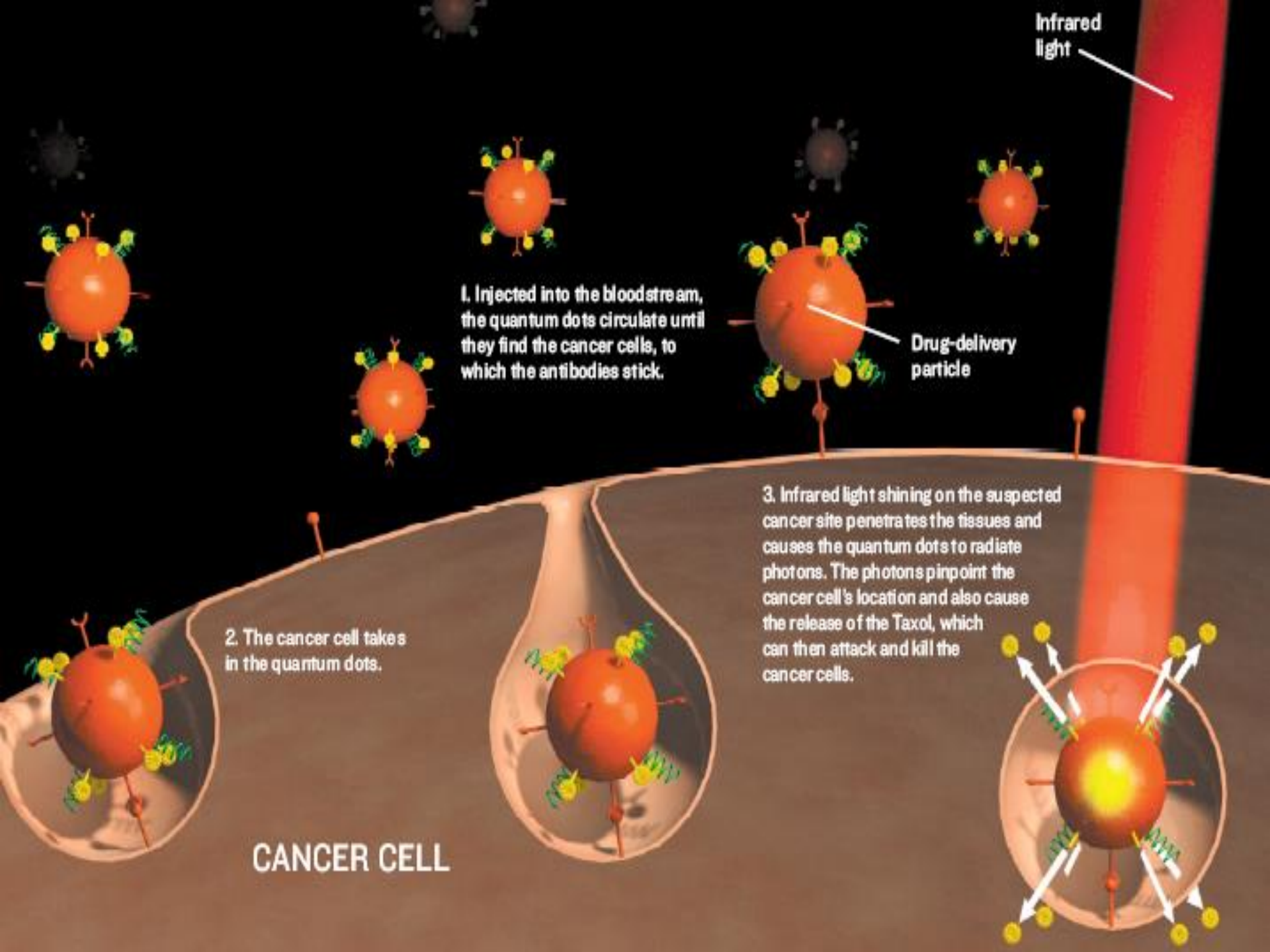
Annu. Rev. Biomed. Eng. 2007. Vol. 9, pp. 257–288

Nature Biotechnology 2003. Vol. 9, pp. 41-46

Quantum Dots

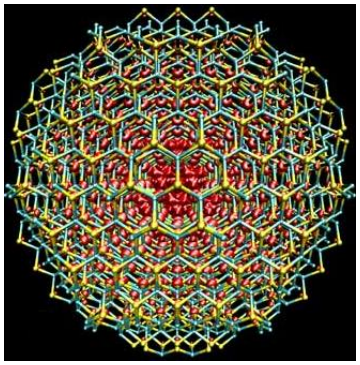





Infrared light
1. Injected into the bloodstream, the quantum dots circulate until they find the cancer cells, to which the antibodies stick.
Drug-delivery particle
2. The cancer cell takes in the quantum dots.
3. Infrared light shining on the suspected cancer site penetrates the tissues and causes the quantum dots to radiate photons. The photons pinpoint the cancer cell's location and also cause the release of the Taxol, which can then attack and kill the cancer cells.
CANCER CELL

Medical Imaging

Optical properties of nanoparticles depend greatly on its structure. Particularly, the color (wavelength) emitted by a quantum dot (a semiconductor nanoparticle) depends on its diameter.



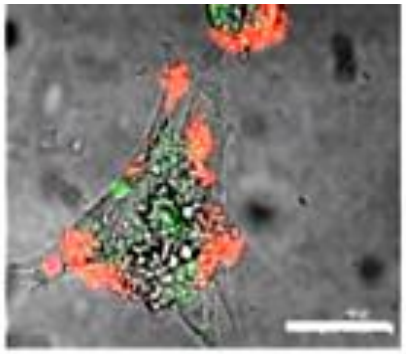
CdSe nanoparticle (QD) structure

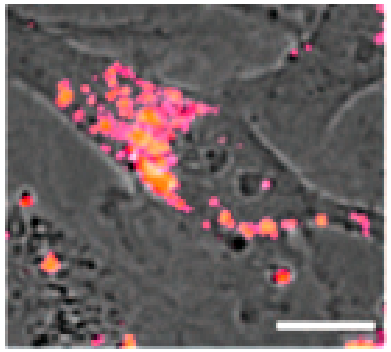
Source: Laurence Livermore Laboratories

Solutions of CdSe QD's of different diameter

Source: Department of immunology, University of Toronto

The quantum dots (QD) can be injected to a subject, and then be detected by exciting them to emit light



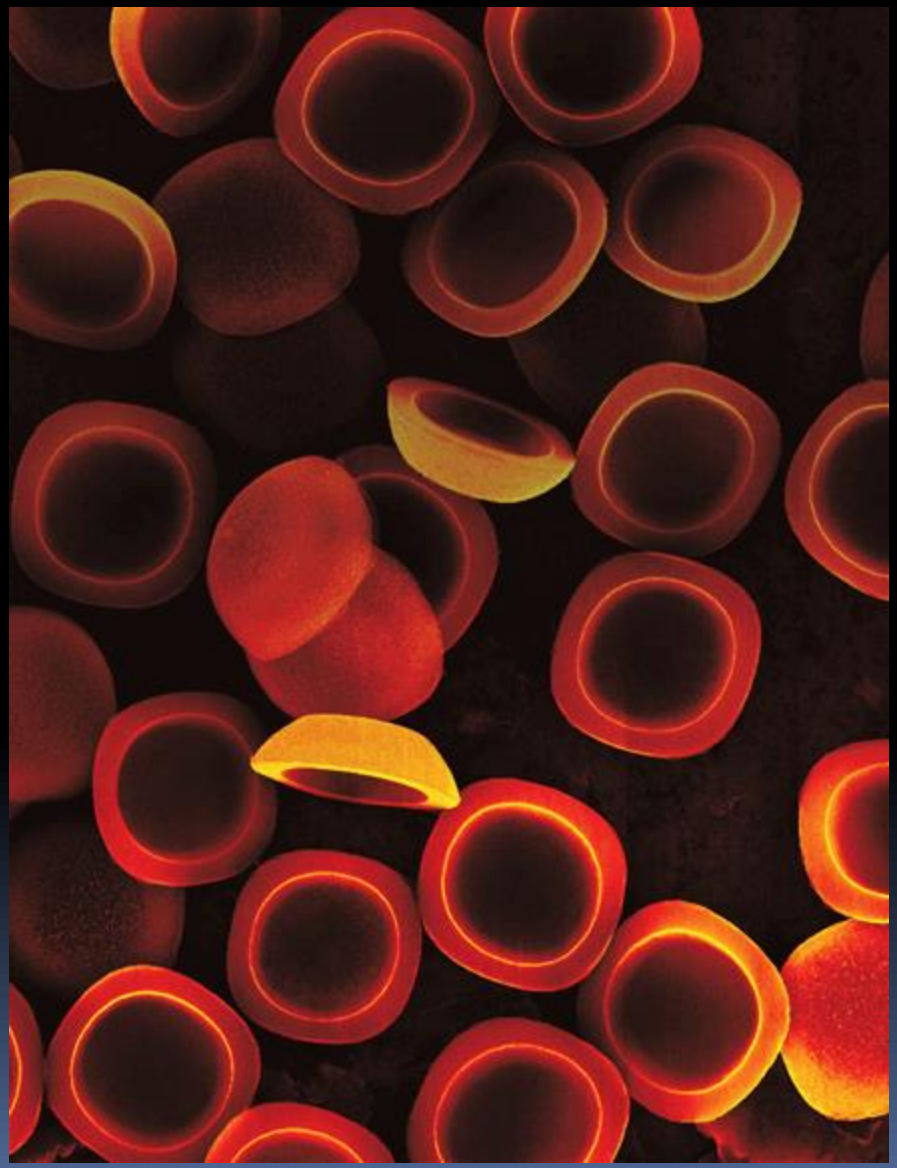


Imaging of QD's targeted on cellular structures

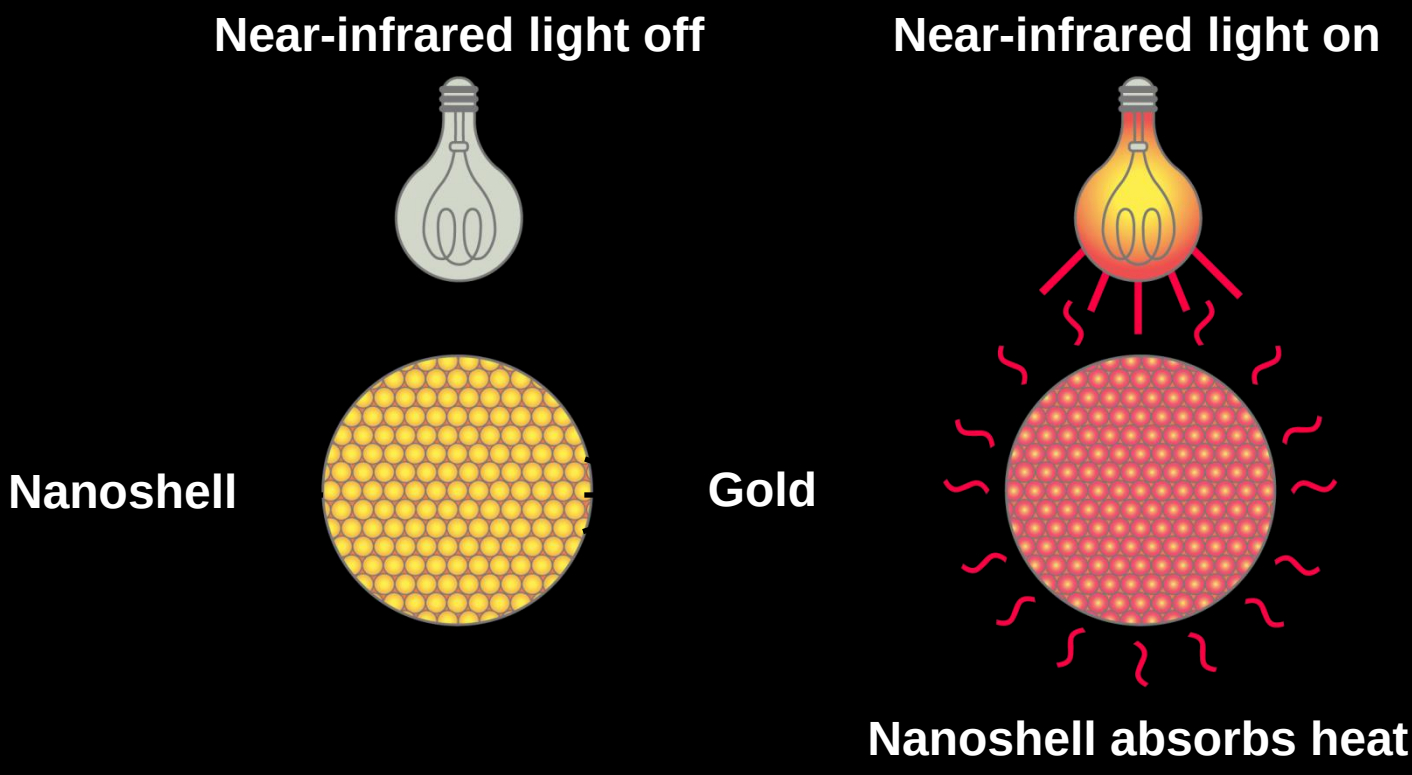
Nano Letters 2008., Vol. 8, pp3887-3892

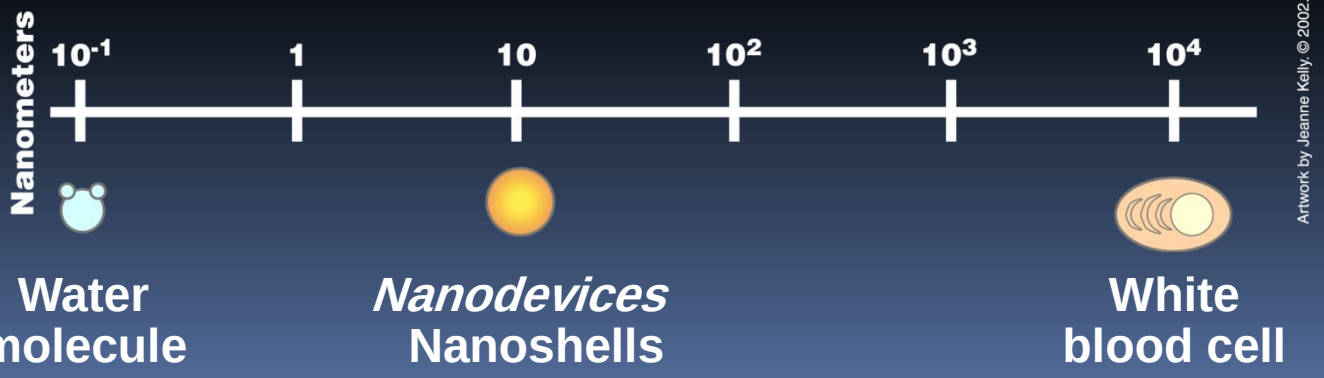
Gold nanoshells

- SiO_2 Core
- 65 nm Size

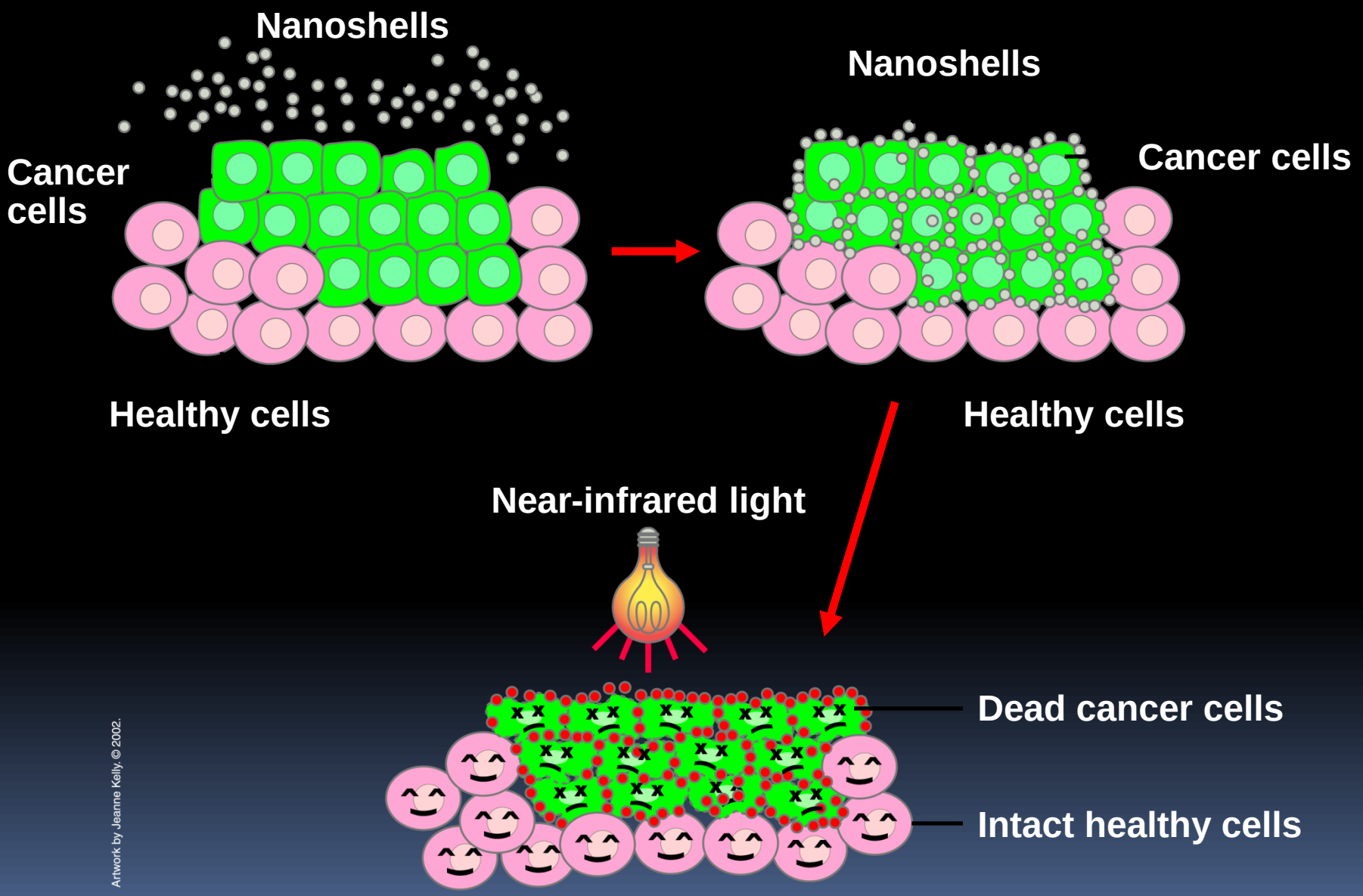


Nanoshells


Near-infrared light off
Near-infrared light on
Nanoshell
Gold
Nanoshell absorbs heat


Nanometers
10^{-1}
1
10
10^2
10^3
10^4
Water molecule
Nanodevices Nanoshells
White blood cell
Artwork by Jeanne Kelly. © 2002.

Nanoshells as Cancer Therapy



Therapy

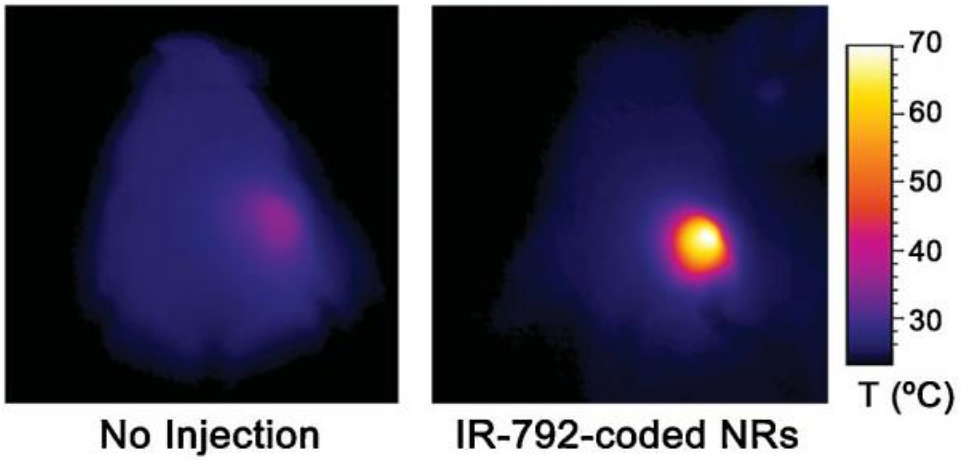
A. Nanometer-sized particles are particularly responsive to electromagnetic and acoustic excitations through a variety of phenomena (e.g. plasmon resonance) that lead to local extreme conditions (e.g. heating). The nanoparticle is able to tolerate this condition, but no so the biological material nearby

Colloidal gold

B. Intramuscular injections of colloidal gold, a suspension of gold nanoparticles, has been used for decades to alleviate pain linked to rheumatoid arthritis. The mechanism is still unknown

Source: John Hopkins Center

C.



An infrared beam illuminates two mice specimens. The local temperature increases for the mouse that received and injection of gold nanorods.

Adv. Mater. 2009, 21, 3175–3180

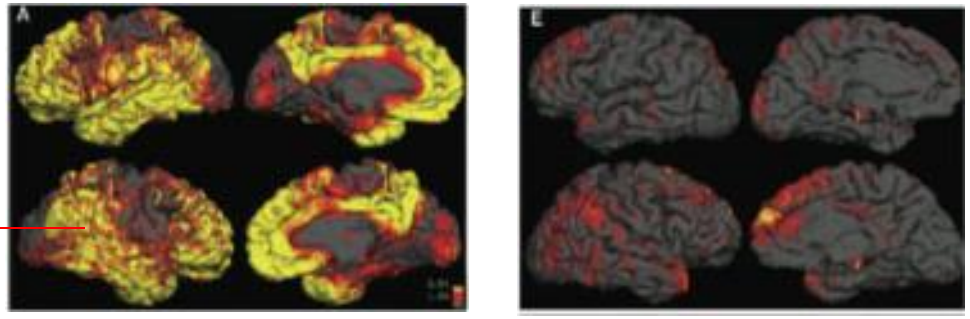
Source: www.wikipedia.com

Gold Nanoparticles vs. Alzheimer

A. Alzheimer and other degenerative diseases are caused my the clustering of amyloidal beta (*Aβ*) protein.

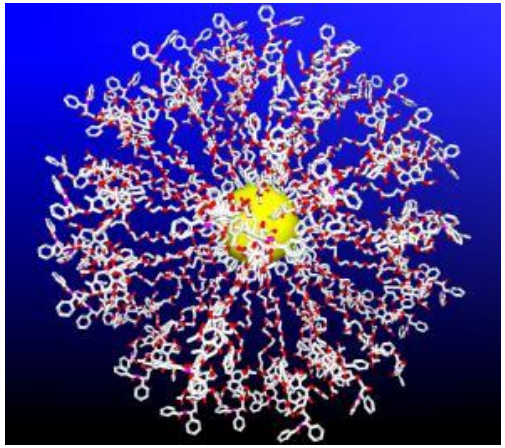
Source: Berkeley Lab

B.



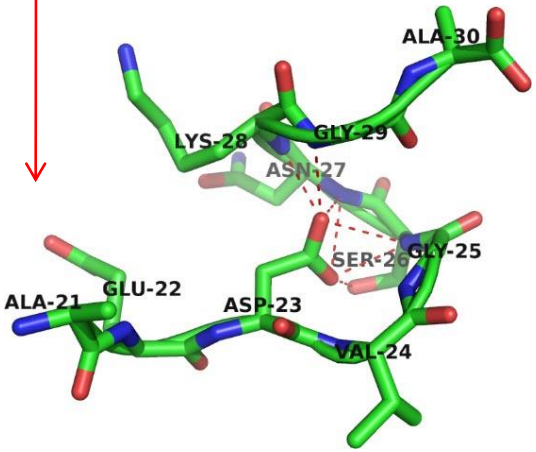
Alzheimer's brain *Healthy brain*

C.



Functionalized nanoparticle

Source: www.internetchemistry.com



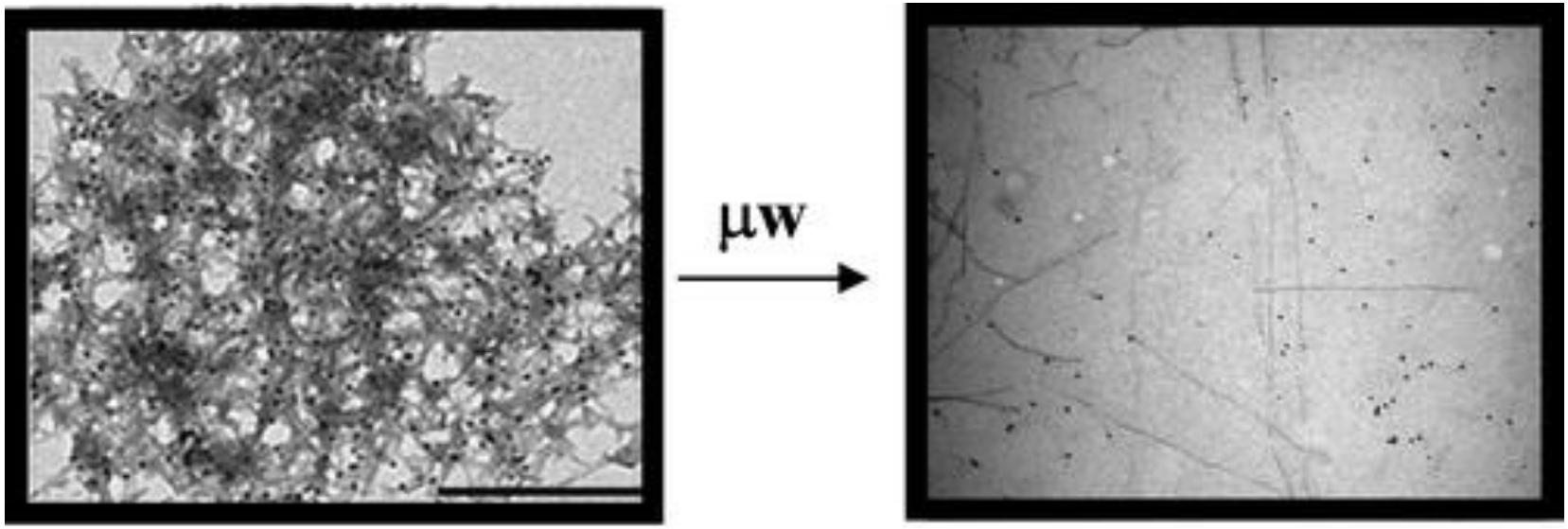
Chemical structure of Aβ-protein

Source: wwwthefutureofthings.com

D. Gold nanoparticles can be functionalized to specifically attach to aggregates of this protein (amyloidosis)

Gold Nanoparticles vs. Alzheimer

A. The functionalized gold nanoparticles selectively attach to the aggregate of amyloidal protein. The microwaves of certain frequency are irradiated on the sample. Resonance with the gold nanoparticles increases the local temperature and destroy the aggregate



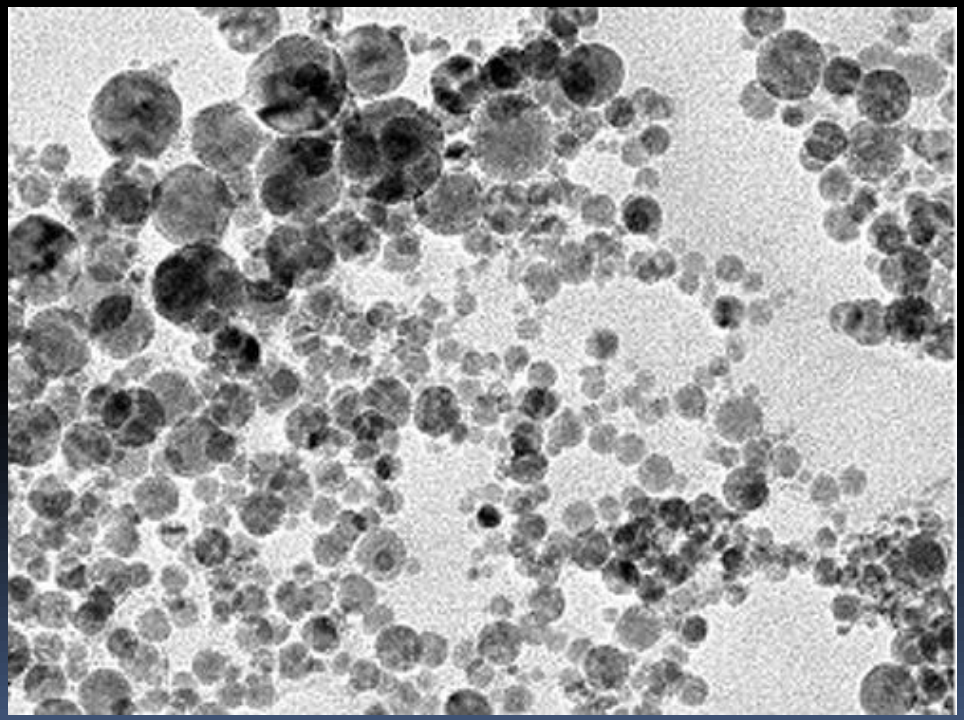
Before irradiation

After irradiation

Nanoletters 2006, Vol. 6, pp.110-115

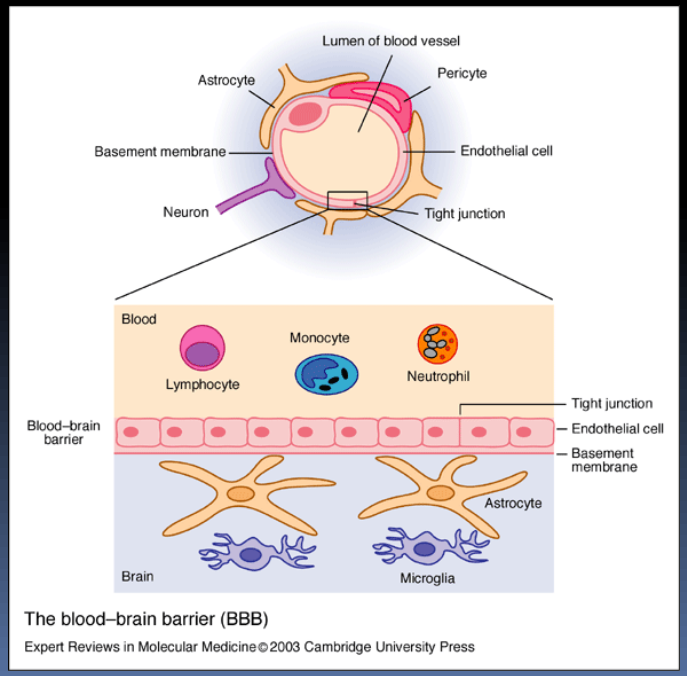
Solid lipid nanoparticles

- Industrial feasibility
- Drug delivery to brain
- Not Toxic



Drug delivery to brain

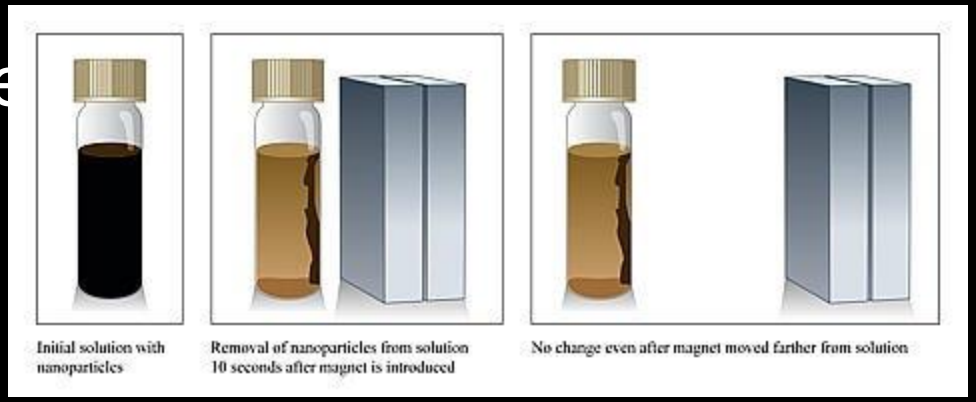
- Specific cells
- Tight junctions in BBB
- Pgp Activity

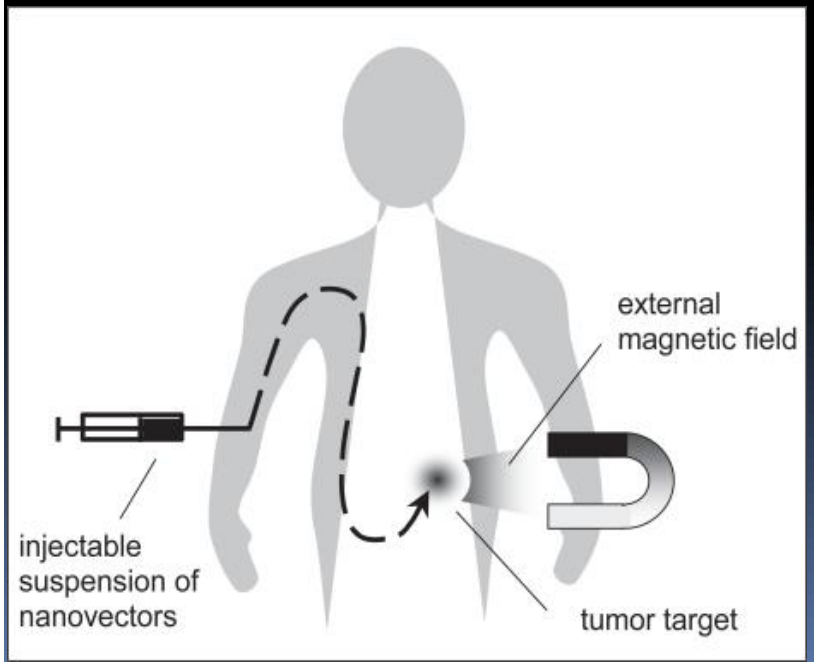


The blood–brain barrier (BBB)

Superparamagnetic NPs

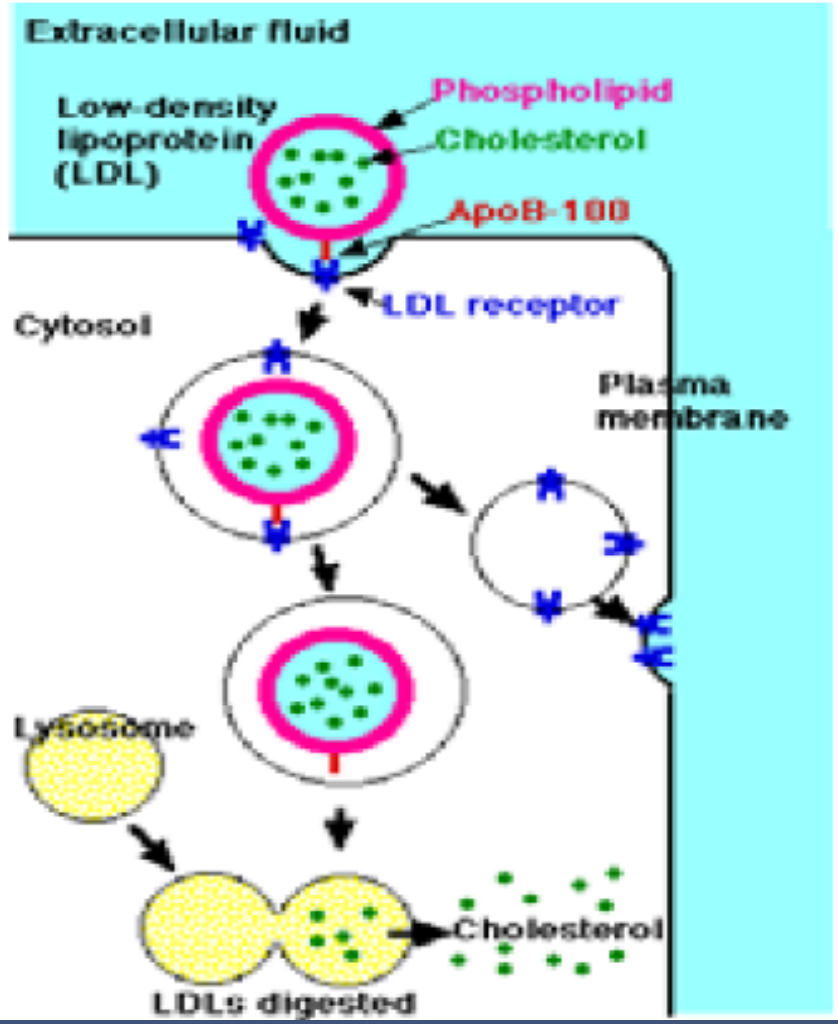
- Easy targe



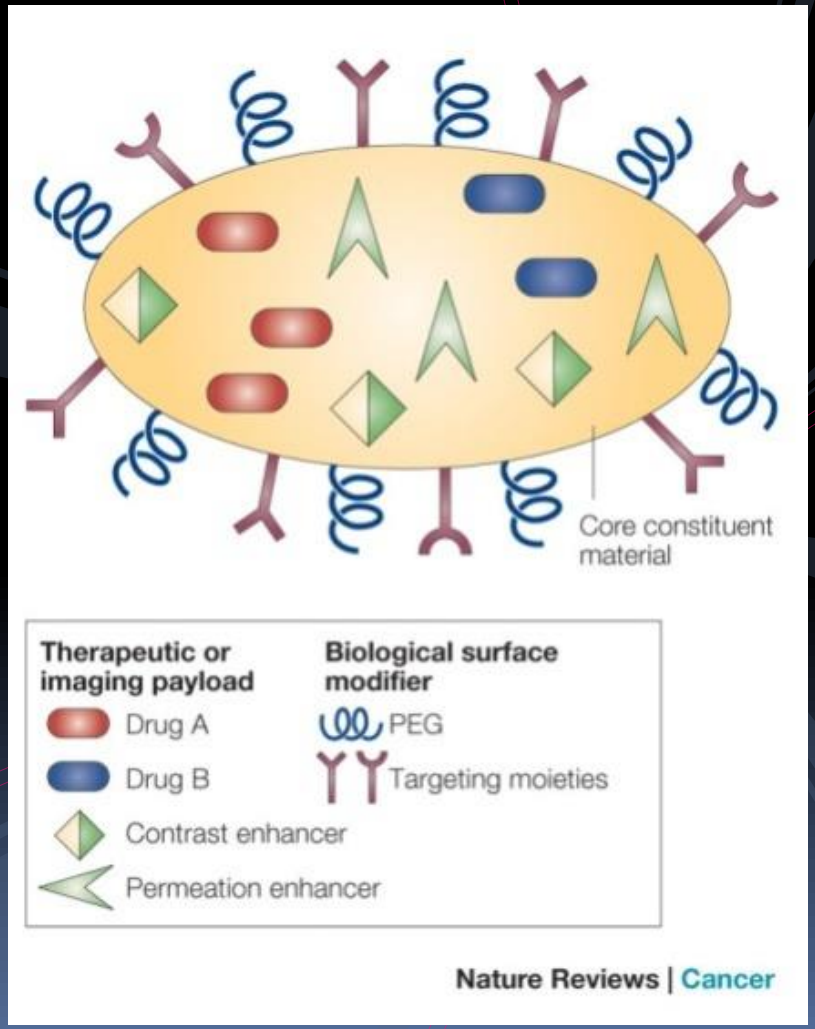


Active Targetting

- Small Molecules
  - Galactose/Glucose/Mannose
  - Folate
- Peptides
  - RGD
- Proteins
  - Transferrin
  - Antibodies
  - LDLs



Active targeting




Thank You!